REMARKS

The amendments herein are made to place the present application in form for allowance, or in the alternative, to place the application in better form for appeal by materially reducing or simplifying the issues for appeal. Claims 1 and 16 are currently amended herein to clarify that the method is used to increase the mammal's production of antigen-specific antibodies or the mammal's innate immunity response to the antigen. Claim 26 was amended simply to put in independent form. The amendments are fully supported by the original claims and specification. No new matter has been added by the amendments made herein. Entry of the amendments at this time is therefore respectfully requested.

Claim 26 was objected to as depending on a rejected claim. Applicant appreciates the Examiner's Acknowledgement that claim 26 would be allowable if written in independent form. Applicant has now amended claim 26 to be in independent form and respectfully requests the Allowance of this claim.

Claim 1, 3, 4, 6, 8, 13, 14, 16, 19, 20, and 23-25 were rejected under 35 U.S.C. 102(b) as being anticipated by Sherr et al. (US 6,407,062) for the reasons set forth on pages 2-4 of the Office Action. Applicant respectfully traverses.

Sherr is directed to the INK4A gene and a mammalian protein (ARF-p19) present during the cell cycle. According to Sherr ARF-p19 expression induced both G1 and G2 phase arrest in rodent fibroblast. Sherr is further directed to the discovery of the unitary inheritance of INK4a-p16 and ARF-p-19 that may reflect a dual requirement for both proteins in cell cycle control. From this understanding, Sherr also teaches the use of the ARF-p19 protein to inhibit the G1 and G2 phase in cancer cells.

In contrast, the presently claimed invention is directed specifically to a method of activating/augmenting the immune system in a mammal (specifically a B cell system response or an innate immunity response to an antigen – in claim 16) to increase the mammal's production of antigen-specific antibodies or the mammal's innate immunity response to the antigen. The presently claimed invention is not directed to a method inhibiting the cell cycle, or more specifically the G1 and G2 phase of the cycle as taught by Sherr. Similarly Sherr is not directed to the presently claimed method of increasing the mammal's production of antigen-specific antibodies or the mammal's innate immunity response to the antigen.

At page 3 of the Office Action, it is pointed out that antibodies used in a composition are sometime labeled with fluorescein isothiocyanate. Sherr states at col. 34, lines 12-13 and 16-17 that "[i]t is also possible to label antibody compositions with a fluorescent compound. . . . Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycoerthrin, phycocyanin, allophycocyanin, o-phthaldehyde, and fluorescamine." The whole purpose of labeling the antibodies in Sherr is to label antibodies for detection purposes only. The fluorescently labeled antibodies disclosed in Sherr do not anticipate the presently claimed invention. In fact, there is nothing in Sherr to teach or suggest the presently claimed method of activating the immune system in a mammal using an "ITC based agent", wherein the ITC is in "an effective amount" to activate or augment an immune response in the mammal to increase the mammal's production of antigen-specific antibodies or the mammal's innate immunity response to the antigen. Both "ITC based agent" and "effective amount" are specifically defined in the present specification.

At paragraph [0032] of the Applicant's application as published it states, "[t]he term 'ITC based agent' refers to compounds wherein isothiocyanate is the base of the compound" and further provides specific examples of ITC based agents, such as, PEITC-NAC or PEITC. The fluorescently labeled antibodies used in Sherr are not ITC based compounds, but are ARF-p19-antibody based compounds that are fluorescently labeled for the purpose of fluorescent detection of the bound and unbound antibody conjugates taught by Sherr (see Col 34, lin341-45). One skilled in the art would know that a label on a antibody or peptide is not the base of the compound, but simply a label. Furthermore, the fluorescent labels are not used to activate the immune system in a mammal to increase the mammal's production of antigen-specific antibodies or the mammal's innate immunity response to the antigen as taught in the presently claimed invention, but simply for detection purposes.

Sherr is directed to ARF-p19F based compounds. In contrast, Applicant's invention is directed to the surprising discovery that when a sufficient quantity of an ITC based agent was administered to a mammal, the ITC based agent activated and/or augmented the immune responses. This was not taught or understood prior to Applicant's discovery. The presently claimed method is directed to this surprising discovery.

At paragraph [0037] of the Applicant's specification as published, an "'effective amount' is defined as an amount of ITC based agent that is capable of producing or increasing an immune

response in a subject." Sherr does not teach use of an "effective amount" of an "ITC based agent" sufficient to activate or augment an immune response in a mammal. Sherr only teaches a sufficient amount of fluorescein isothiocyanate to effectively label antibodies for detection purposes to detect bound and unbound antibodies.

At paragraph [0043] of the Applicant's specification as published, the term "augment" is also defined as enhancing and/or increasing the immune response in a mammal as compared to the immune response prior to treatment with the "ITC based agent."

Sherr does not concern and is not directed to a method of activating or increasing the immune response in a mammal to increase the mammal's production of antigen-specific antibodies or the mammal's innate immunity response to the antigen as compared to the immune response prior to administration of the effective amount of "ITC based agent."

Furthermore, Sherr does not disclose the specific embodiments of the presently claimed invention as set forth in dependent claims 3, 4, 6, 8, 13-14, 19-20, and 23-25, either. For example, Sherr does not teach a method of activating a B cell system response to a specific antigen or an innate immunity using an ITC-based agent (see claims 3 and 4); or a method of treating a patient having an immunodeficiency or an infection, more specifically, AIDS or SARS, by using an ITC-based agent to activate or increase the subjects immune response (see claims 6 and 7). Sherr does teach treating cancer using ARF-p19 protein to inhibit the G1 and G2 phase in cancer cells, but does not teach a method of treating cancer using an ITC based agent in an effective amount sufficient to activate a B cell immune system for the production of one or more antibodies specific to a cancer cell antigen, and further does not teach such a method wherein the mammal's own B and NK cell numbers are increased (see Claims 8, 18, and 19). Sherr fails to teach a method of increasing a mammals' production of antigen-specific antibodies or innate immunity response to an antigen as presently claimed.

As the courts have made clear, a claim can only be anticipated if each and every element as set forth in the claim is found in a single prior art reference. (See *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)).

As all of the element of the presently claimed invention are not taught by Sherr as explained above, Applicant respectfully requests that this rejection be withdrawn.

Claim 1, 6-8, 10-14, 16, 19 and 21-22 were rejected under 35 U.S.C. 102(b) as being anticipated by Moore et al. (US 2002/0164694) for the reasons set forth on pages 4-5 of the Office Action. Applicant respectfully traverses.

Moore is directed to IRF3 polypeptides. In particular, IRF3 polypeptides to treat, prevent or ameliorate infectious diseases. The Office Action, cites page 42, paragraph 254 of Moore as the bases of the rejection, specifically citing the mention of fluorescein isothiocyanate. Like Sherr, the only mention of an isothiocyanate is the compound for fluorescein isothiocyanate used to fluorescently label an antibody. At paragraph [0325] of Moore it explains that some of the most commonly used fluorescent labeling compounds for detection purposes includes fluorescein isothiocyanate. This in no way teaches or discloses the presently claimed method.

As explained above, the fluorescently labeled antibodies disclosed here in Moore do not anticipate the presently claimed invention. In fact, there is nothing in Moore that teaches or suggests the presently claimed, i.e., the method of activating the immune system in a mammal using an "ITC based agent," wherein the ITC is in "an effective amount" to activate or augment an immune response in the mammal to increase the mammal's production of antigen-specific antibodies or innate immunity response to the antigen. Both "ITC based agent" and "effective amount" are specifically defined in the present specification as explained above. "The term 'ITC based agent' refers to compounds wherein isothiocyanate is the base of the compound," e.g., PEITC-NAC or PEITC.

In contrast to the presently claimed invention, the fluorescently labeled antibodies used in Moore are not ITC based compounds, but are IRF3 polypeptides/antibodies based compounds that are fluorescently labeled for the purpose of fluorescent detection of bound and unbound IRF3 antibody conjugates. One skilled in the art would know that a label is not the base of the compound. Furthermore, the fluorescent labels are not used to activate the immune system to cause a immune response in a mammal to increase the mammal's production of antigen-specific antibodies or the mammal's innate immunity response to the antigen as presently claimed, but are simply used for detection purposes.

Moore is directed to IRF3 polypeptide based compounds, not ITC based agents. Applicant's invention is directed to the surprising discovery that when a sufficient quantity of an ITC based agent is administered to a mammal, the ITC based agent activated and/or augmented the immune responses in the mammal and caused a quantitatively increase in the number of

mammalian produced antibodies specific to a particular antibody. This was not taught or understood prior to Applicant's discovery. The presently claimed method is directed to this surprising discovery.

Also, as explained above, an "'effective amount' is defined as an amount of ITC based agent that is capable of producing or increasing an immune response in a subject." Moore does not teach use of an "effective amount" of a ITC based agent sufficient to activate or augment an immune response in a mammal. The only mention of an isothiocyanate in Moore is the specific compound fluorescein isothiocyanate used for the purpose of fluorescently labeling antibodies for detection purposes.

In addition, Moore does not disclose the specific embodiments of the presently claimed method as set forth in dependent claims 6-8, 10-14, 19 and 21-22. For example, Moore does not teach a method of activating a B cell system response to a specific antigen or an innate immunity using an ITC-based agent (see claims 3 and 4); or a method of treating a patient having an immunodeficiency or an infection, more specifically, AIDS or SARS, by using an ITC-based agent to activate or increase the subjects immune response (see claims 6 and 7).

The only mention in Moore of an isothiocyanate is the compound for fluorescein isothiocyanate for the sole purpose of fluorescently labeling antibodies. For all the reasons previously mentioned, Moore does not teach use of an "ITC-based agent" as defined by the specification. This is evident by the fact that the fluorescein isothiocyanate is used solely for detection purposes only, not to activate or increase the immune response in the mammal sufficiently to increase the quantity of the mammal's antibodies specific to a particular antigen or to increase the mammal's innate immunity response to the antigen.

For these reasons explained above, Applicant respectfully requests that this rejection be withdrawn.

Claim 2, 15, 17, and 27-28 were rejected under 35 U.S.C. 103(a) as being unpatentable over Sherr et al. (US 6,407,062) as applied to claims 1, 3, 4, 6, 8, 13, 14, 16, 19, 20, and 23-25 above and in view of Ghai et al. (US 5,955,269) for the reasons set forth on pages 6-8 of the Office Action. Applicant respectfully traverses.

As explained above, Sherr is directed to the INK4A gene and a mammalian protein (ARF-p19) present during the cell cycle. According to Sherr ARF-p19 expression induced both G1 and G2 phase arrest in rodent fibroblast. Sherr is further directed to the discovery of the

unitary inheritance of INK4a-p16 and ARF-p-19 that may reflect a dual requirement for both proteins in cell cycle control. From this understanding, Sherr also teaches the use of the ARF-p19 protein to inhibit the G1 and G2 phase in cancer cells.

In contrast, the present invention is directed specifically to a method of activating/augmenting the immune system in a mammal (specifically a B cell system response or an innate immunity response to an antigen – in claim 16) to increase the mammal's production of antigen-specific antibodies or the mammal's innate immunity response to the antigen, not a method inhibiting the cell cycle, or more specifically the G1 and G2 phase of the cycle.

Sherr does not teach administration to a mammal of an "effective amount" of an "ITC based agent" sufficient to activate or augment n immune response in the mammal. Sherr only teaches a sufficient amount of fluorescein isothiocyanate to effectively label antibodies for detection purposes to detect bound and unbound antibodies. Furthermore as stated in the Office Action, Sherr also does not teach use of an ITC based agent (PEITC-NAC or PEITC; claims 2, 17, 27, and 28) or wherein the ITC-based agent is administered systemically in a dietary composition or supplement (claim 15).

Ghai fails to remedy the deficiencies of Sherr. Ghai is directed to an assay system for screening for nutraceuticals. Ghai fails to teach the presently claimed invention as well. Furthermore, one skilled in the art would not be motivated to combine the teachings of Sherr with the teachings of Ghai and even if they were combined they would not make obvious the presently claimed invention.

While Ghai does mention the identification of phenethyl isothiocyanate isolated from watercress it does mention the use of a ITC based agent as presently claimed. Furthermore, one skilled in the art would not be motivated to substitute the fluorescein isothiocyanate used as a fluorescent label mentioned in Sherr with the nutraceuticals mentioned in Ghai as they would not function for the same purpose – as a fluorescent label. If one of Ghai's nutraceuticals were used in place of the conjugated fluorescein isothiocyanate taught in Sherr the conjugate would not properly function to detect bound or unbound antibodies as taught by Sherr.

There is also no motivation to substitute the ARF-p19 based compounds taught in Sherr with a the compounds taught by Ghai, as there is no indication that these compounds would have the same function as ARF-p19, i.e., that they would effectively inhibit the G1 and G2 phase in cancer cells.

Thus, Sherr alone or combined with Ghai fails to make obvious the presently claimed invention as set forth in the independent claims or the more specific dependent claims. Applicant, therefore respectfully requests that this rejection be withdrawn.

Claim 2, 15, 17, and 20 were rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al. (US 2002/0164694) as applied to claims 1, 6-8, 10-14, 16, 19 and 21-22 above and in view of Ghai et al. (US 5,955,269) for the reasons set forth on pages 8-10 of the Office Action. Applicant respectfully traverses.

As explained above, Moore is directed to IRF3 polypeptides. In particular, IRF3 polypeptides to treat, prevent or ameliorate infectious diseases. Like Sherr, the only mention of an isothiocyanate is the compound for fluorescein isothiocyanate used as a fluorescent compound for detection purposes. At paragraph [0325] of Moore it explains that some of the most commonly used fluorescent labeling compounds for detection purposes includes fluorescein isothiocyanate. This in no way teaches or discloses the presently claimed method.

Moore does not teach administration to a mammal of an "effective amount" of an "ITC based agent" sufficient to activate or augment n immune response in the mammal. Sherr only teaches a sufficient amount of fluorescein isothiocyanate to effectively label antibodies for detection purposes to detect bound and unbound antibodies. Furthermore as stated in the Office Action, Sherr also does not teach use of an ITC based agent (PEITC-NAC or PEITC; claims 2, 17, 27, and 28) or wherein the ITC-based agent is administered systemically in a dietary composition or supplement (claim 15).

Ghai fails to remedy the deficiencies of Moore. Ghai is directed to an assay system for screening for nutraceuticals. Ghai fails to teach the presently claimed invention as well. Furthermore, one skilled in the art would not be motivated to combine the teachings of Sherr with the teachings of Ghai and even if they were combined they would not make obvious the presently claimed invention.

While Ghai does mention the identification of phenethyl isothiocyanate isolated from watercress it does mention the use of a ITC based agent as presently claimed. Furthermore, one skilled in the art would not be motivated to substitute the fluorescein isothiocyanate used as a fluorescent label mentioned in Moore with the nutraceuticals mentioned in Ghai as they would not function for the same purpose – as a fluorescent label. If one of Ghai's nutraceuticals were

used in place of the conjugated fluorescein isothiocyanate taught in Moore the conjugate would not properly function to detect bound or unbound antibodies as taught by Moore.

Thus, Moore alone or combined with Ghai fails to make obvious the presently claimed method of increasing the mammal's production of antigen-specific antibodies or the mammal's innate immunity response to the antigen. Applicant, therefore respectfully requests that this rejection be withdrawn.

Claim 5, 9, and 18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Sherr et al. (US 6,407,062) as applied to claims 1, 3, 4, 6, 8, 13, 14, 16, 19, 20, and 23-25 above and in view of Horan et al. (US 5,665,328), for the reasons set forth on pages 10-11 of the Office Action. Applicant respectfully traverses.

Again, Sherr is directed to the INK4A gene and a mammalian protein (ARF-p19) present during the cell cycle. According to Sherr ARF-p19 expression induced both G1 and G2 phase arrest in rodent fibroblast. Sherr is further directed to the discovery of the unitary inheritance of INK4a-p16 and ARF-p-19 that may reflect a dual requirement for both proteins in cell cycle control. From this understanding, Sherr also teaches the use of the ARF-p19 protein to inhibit the G1 and G2 phase in cancer cells.

In contrast, the present invention is directed specifically to a method of activating/augmenting the immune system in a mammal (specifically a B cell system response or an innate immunity response to an antigen – in claim 16), not a method inhibiting the cell cycle, or more specifically the G1 and G2 phase of the cycle.

Sherr also does not teach a method wherein the ITC-based agent activates or augments a NK cell system as set froth at page 10 of the Office Action.

Horan fails to remedy the deficiencies of Sherr. Horan is directed to compounds and methods for binding bio-affecting substances to the surface membrane of bio-particles, such as eukaryotic cells. The only mention of an isothiocyanate in Horan is for purposes of Fluorescent labeling techniques (fluorescein isothiocyanate) and as a functional group for linking compounds, for example to link a fluorescein isothiocyanate to an antibody.

Like Sherr, Horan fails to teach or suggest the presently claimed method. Horan does not teach or suggest the administration of "an effective amount" of a "ITC based agent" to a mammal to activate or augment the mammal immune response to increase the mammal's

production of antigen-specific antibodies or the mammal's innate immunity response to the antigen.

Furthermore, there is no motivation to combine the Horan with Sherr as suggested by the examiner. Even if you combined Sherr with Horan, you would not get the presently claimed invention, but ARF-p19 based compounds and conjugated that inhibit the G1 and G2 phase in cancer cells.

As Sherr and Horan fail to teach or suggest the presently claimed invention, alone or combined, Applicant respectfully requests that this rejection be withdrawn.

In view of the above, Applicant believes all claims to be in condition for allowance. If there are any questions, the Examiner is invited to call Applicant's representative Rodney Fuller at (602) 916-5404 to resolve any remaining issues to expedite the allowance of this application.

Respectfully submitted,

July 16, 2007
Date

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